Remarks/Arguments

Claim 1 is amended. Claims 1-18 are pending in the application. Support for the amendments can be found at paragraphs 11and 83 of the specification in U.S. Pub. No. 2006/0089587A1. Reexamination and reconsideration of the application, as amended, are respectfully requested.

Double Patenting

Claims 1-3, 6-7, and 16 stand provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-3, 5-7,and 9-11 of co-pending U.S. Patent Application No. 11/718,386. Applicants respectfully request that the rejection be held in abeyance until the pending claims in either application are found to be otherwise allowable except for this ground of rejection.

Claim Rejections Under 35 USC § 103

Claims 1-7 and 9-18 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hajime (JP Pub. No. 07-136256) as evidenced by Tani, et al., (U.S. Pat. No. 4,576, 928. Applicant respectfully traverses this rejection.

Claim 1 as amended is as follows:

> An adsorbent capable of whole blood treatment for adsorbing low-density lipoproteins and fibrinogen, the adsorbent comprising a tryptophan derivative and a polyanionic compound which are immobilized on a water-insoluble porous carrier, wherein the amount of the immobilized polyanionic compound is 0.10 μmol to 1.5 μmol per milliliter of wet volume of the adsorbent, and the

molar ratio of the amount of the immobilized tryptophan derivative to the amount of the immobilized polyanionic compound is 1 to 70; wherein said adsorbent is capable of whole blood treatment without separation of the plasma and said adsorbent specifically adsorbs low-density lipoproteins and fibrinogen.

Applicant respectfully submits that Hajime and Tani fail to disclose or teach at least the following as set forth by claim 1: 1) an adsorbent capable of whole blood treatment without plasma separation and 2) a molar ratio of 1 to 70 of tryptophan to polyanionic compound.

On the point of an adsorbent capable of whole blood treatment without plasma separation as set forth by claim 1, Hajime in contrast discloses methods and devices capable of decreasing the viscosity of *plasma* by removing fibrinogen and LDL (abstract; paragraphs 1, 5, 7, & 15). Hajime specifically discloses the treatment of plasma and not whole blood and does not teach or suggest that its disclosed methods and devices that are used to treat plasma may be used to treat whole blood. It is well known in the art that whole blood contains many more components than plasma and that it is easier to remove fibrinogen and LDL from plasma than from whole blood. MPEP 2143.02 makes it clear that there must be a reasonable expectation of success in the modification or combination suggested by the Office. At the time of the invention, there would not have been any reasonable expectation of success that the adsorber used to remove fibrinogen and LDL from plasma could successfully be used to remove fibrinogen and LDL from whole blood. An adsorber that works for whole blood may not work for plasma, and vice versa, and the Office has not made any showings of such. Further, Hajime teaches away from using whole blood, as the preferred method for using the adsorbent is when the plasma is separated from the whole blood (Applicants specification at paragraph

7). As such, it would not have been obvious to one of skill in the art to use the device of Hajime to treat whole blood, as set forth by claim 1.

Tani claims that its adsorbent removes a variety of substances including proteins, viruses and harmful cells from plasma or blood (abstract and col. 1, ll. 65 to col. 2, ll. 7). Tani exemplifies the removal of a wide array of VLDL and/or LDL; IgG, C_{1q} or haptoglobin; endotoxin; rheumatoid factor; anti-DNA antibody or DNA; and anti-acetylcholine receptor antibody from plasma (i.e., plasma derived from familial hypercholesterolemia, normal human plasma, normal human plasma containing about 100 μg/ml of a commercially available endotoxin, human plasma derived from rheumatism, human plasma derived from systemic lupus erythematosus and human plasma derived from myasthenia gravis), while Applicants adsorber removes only LDL and fibrinogen from whole blood As such, it would not be obvious to combine or suggest that an adsorber that removes a wide variety of components may function or comprise the same components as an adsorber that only removes LDL and fibrinogen.

Moreover, while Tani discloses that its adsorbent removes a variety of substances including proteins, viruses and harmful cells from plasma or blood (abstract and col. 1, ll. 65 to col. 2, ll. 7), all of the exemplary adsorbents disclosed in Tani are tested using plasma only, and none are tested using whole blood (col. 14, ll. 24 to Col. 18, ll. 22). Tani is silent as to whether the adsorbent is capable of whole blood treatment.

Plasma and whole blood have different characteristics, and plasma does not contain leukocytes or platelets. One of ordinary skill in the art would understand that an adsorbent capable of treating only plasma would not necessarily also treat whole blood. To suggest otherwise is impermissible hindsight.

And there is no teaching or suggestion in any of the cited art that an adsorber that removes a wide variety of components from plasma only may function or

comprise the same components as an adsorber that only removes LDL and fibrinogen from whole blood.

On the point of an adsorbent comprising a molar ratio of 1 to 70 of tryptophan to polyanionic compound set forth by claim 1, as the Office has pointed out, Hajime does not expressly disclose the molar ratio of tryptophan to polyanionic compound of 1 to 70, and Applicant respectfully submits that Hajime consequently does not expressly disclose an adsorbent capable of treating whole blood whose molar ratio of tryptophan to polyanionic compound is 1 to 70. Moreover, Applicant respectfully submits that Tani also does not expressly disclose the molar ratio of tryptophan to polyanionic compound of 1 to 70 in its adsorbent. As such, it would not be obvious to combine or suggest the molar ratio of tryptophan to polyanionic compound of 1 to 70 in an adsorbent capable of whole blood treatment.

In view of the foregoing, Hajime as evidenced by Tani is not obvious over present claim 1. Likewise, dependent claims 2-7 and 9-18 are also patentable over Hajime as evidenced by Tani for at least the same reasons as claim 1. With respect to claim 2, Hajime in its Comparative Example 1 discloses that an adsorbent having dextran sulfate immobilized to the carrier can adsorb LDL or VLDL, but it does not have the capability to adsorb fibrinogen. Hajime also explains that such adsorbent would have a very high level of activated blood kinin 1/ which is not a desirable effect for practical reasons (paragraph 18). Therefore, Hajime teaches away from an adsorbent comprising dextran sulfate immobilized on the water-insoluble porous carrier as featured in claim 2, and for this reason as well, claim 2 is also patentable over Hajime. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

1/ Note: The machine translation of Hajime refers to "blood quinine" but this is translation error, as the Japanese original refers to "blood kinin."

Claim 8 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Hajime in view Kuroda, et al., (U.S. Pat. No. 5,286,449) of as evidenced by Tani. Applicant respectfully traverse this rejection.

Claim 8 depends from claim 1, and as such includes all the limitations thereof, and is therefore patentable over Hajime for at least the same reasons discussed above with regard to claim 1.

Kuroda is not seen to remedy the defects of Hajime and is cited for its relevance regarding the capacity of the adsorber. As such, the combined teachings of the prior art fail to teach or suggest each element of the claimed invention. Thus, the combination suggested by the Office cannot render the claimed invention obvious.

The Examiner indicates that it would have been obvious to one skilled in the art to modify the Hajime device to include Kuroda's adsorber capacity. MPEP 2143.02 makes it clear that there must be a reasonable expectation of success in the modification or combination suggested by the Office. At the time of the invention, there would not have been any reasonable expectation of success that the adsorber used to remove fibrinogen and LDL from plasma could successfully be used at the same capacity as an adsorber used for whole blood. As an adsorber that works for whole blood may not work for plasma and the Office has not made any showing of such.

Accordingly, Hajime in view of Kuroda as evidenced by Tani is not obvious over the present claim 8. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

Claims 1-4, 6-12, and 18 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Kuroda ('449) as evidenced by Tani. Applicant respectfully traverses this rejection.

Applicant respectfully submits that Kuroda as evidenced by Tani fails to disclose or teach at least the following as set forth by claim 1: 1) an adsorbent capable of specifically adsorbing low-density lipoproteins (LDL) and fibrinogen without plasma separation and 2) a molar ratio of 1 to 70 of tryptophan to polyanionic compound.

On the point of an adsorbent capable of specifically adsorbing low-density lipoproteins (LDL) and fibrinogen without plasma separation as set forth by claim 1, Kuroda in contrast discloses an adsorber that adsorbs malignant components such as autoantibodies and immune complexes, low or very low density lipoproteins (LDL or VLDL) and substances of middle or low molecular weights which are increased by liver diseases (col. 1, ll. 43-51; col. 16, ll. 47-50; and col. 17, ll. 46-50). The adsorber comprises blood introduction and withdrawal means and a plurality of porous hollow fibers. Each porous hollow fibers comprise a membranous porous resin matrix with pores that open to the inner wall of the hollow fiber and a plurality of ligands linked to the overall surface of the resin (col. 1, ll. 11-22; col. 4, ll. 1-39). Even though the adsorber module allows for the entry of whole blood into it, the plasma is separated from the blood when it flows inside of the porous hollow fibers (col. 5, ll. 32-39 & 64-68; col. 6, ll. 1-24; Example 1 [col. 16, ll. 7-12]; Example 2 [col. col. 17, ll. 21-22]; Examples 3 to 5 [col. 18, ll. 34-36]) . The malignant components, such as autoantibody and an immune complex (col. 9, ll. 56-59), are adsorbed to the porous hollow fibers as the plasma separates from the blood and then again when the plasma is rejoined with the blood. As such, it would not be obvious to combine or suggest that an adsorber that removes a wide variety of components and separates the plasma from the whole blood may function or comprise the same

components as an adsorber that only removes LDL and fibrinogen and does not separate the plasma from the whole blood.

Tani discloses an adsorbent that removes a variety of substances including proteins, viruses and harmful cells from plasma or blood (abstract and col. 1, ll. 65 to col. 2, ll. 7). Tani exemplifies the removal of a wide array of VLDL and/or LDL; IgG, C_{1q} or haptoglobin; endotoxin; rheumatoid factor; anti-DNA antibody or DNA; and anti-acetylcholine receptor antibody from plasma (i.e., plasma derived from familial hypercholesterolemia, normal human plasma, normal human plasma containing about 100 μg/ml of a commercially available endotoxin, human plasma derived from rheumatism, human plasma derived from systemic lupus erythematosus and human plasma derived from myasthenia gravis), while Applicants adsorber removes only LDL and fibrinogen from whole blood As such, it would not be obvious to combine or suggest that an adsorber that removes a wide variety of components may function or comprise the same components as an adsorber that only removes LDL and fibrinogen.

On the point of an adsorbent comprising a molar ratio of 1 to 70 of tryptophan to polyanionic compound as set forth by claim 1, Kuroda merely specifies a preferred molecular weight of tryptophan and dextran sulfate (Col. 10, ll. 9 to Col. 11, ll 19), and it does not disclose or suggest immobilizing both tryptophan and dextran sulfate on the carrier. The molar ratio of 1 to 70 of tryptophan to polyanionic compound set forth in claim 1 refers to the ratio of these substances which are both immobilized on a water-insoluble porous carrier. The concepts of immobilization amount as set forth in claim 1 and the molecular weight of the individual substances used in Kuroda's adsorber are clearly not the same, and one does not necessarily directly correlate to the other.

Specifically, Kuroda does not disclose or suggest immobilizing both tryptophan and dextran sulfate on a carrier. Example 2 of Kuroda only has dextran

sulfate immobilized on the carrier, and it does not have any tryptophan immobilized on the carrier. Moreover, Kuroda does not speak on the immobilization amount of dextran sulfate that is immobilized on an adsorbent. Example 1, which is incorporated by Example 2, only describes one example in which 360 µmol/g of trypotophan is immobilized, and Example 1 does not have any dextran sulfate immobilized on the carrier. Furthermore, Example 1 of Kuroda adsorbs rheumatoid factors and immune complex (col. 16, ll. 47-50), not fibrinogen as in the Applicant's invention.

Therefore, Applicant respectfully submits that Kuroda does not disclose or suggest an adsorbent comprising a molar ratio of 1 to 70 of tryptophan to polyanionic compound as set forth by claim 1. Tani fails to cure the defect of Kuroda, as it also does not disclose or teach an adsorbent comprising a molar ratio of 1 to 70 of tryptophan to polyanionic compound as set forth in claim 1. Tani also does not disclose or suggest that immobilizing tryptophan derivative on the carrier in the adsorbent would enable removing fibrinogen from the treated substance. As such, it would not be obvious to combine or suggest an adsorbent comprising tryptophan of a certain molecular weight or polyanionic compound of certain molecular weight may function or comprise the same components as the adsorbent comprising molar ratio of 1 to 70 of immobilized tryptophan to immobilized polyanionic compound as set forth in claim 1.

In view of the foregoing, Kuroda as evidenced by Tani is not obvious over present claim 1. Likewise, dependent claims 2-4, 6-12, and 18 are also patentable over Kuroda for at least the same reasons as claim 1. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

Claims 5 and 13-17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Kuroda ('449) as evidenced by Tani and Kuroda (U.S. Pat. No. 4,627,915). Applicant respectfully traverses this rejection.

Claim 5 depends from claim 1, and as such includes all the limitations thereof, and is therefore patentable over Kuroda for at least the same reasons discussed above with regard to claim 1.

Tani as discussed above nor Kuroda ('915) is not seen to provide evidence needed to remedy the defects of Kuroda ('449). Kuroda ('915) discloses an adsorbent that adsorbs autoantibodies and immune complexes (abstract). Adsorbtion occurs through the separation of the plasma from the blood, once the blood is inside of the adsorber (abstract). As such, the teachings and evidence of the prior art fail to teach or suggest each element of the claimed invention.

Accordingly, Kuroda ('449) as evidenced by Tani and Kuroda ('915) is not obvious over the present claim 5 and 13-17. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

Claims 1-6 and 9-16 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Tani, et al. Applicant respectfully traverses this rejection.

Applicant respectfully submits that Tani fails to disclose or teach at least the following as set forth by claim 1: 1) an adsorbent capable of specifically adsorbing low-density lipoproteins (LDL) and fibrinogen without plasma separation and 2) a molar ratio of 1 to 70 of tryptophan to polyanionic compound. In contrast, Tani discloses adsorbent that removes a variety of substances including proteins, viruses and harmful cells from plasma or blood (abstract and col. 1, ll. 65 to col. 2, ll. 7). Tani exemplifies the removal of a wide array of VLDL and/or LDL; IgG, C_{1q} or haptoglobin; endotoxin; rheumatoid factor; anti-DNA antibody or DNA; and anti-acetylcholine receptor antibody from plasma (i.e., plasma derived from familial hypercholesterolemia, normal human plasma, normal human plasma containing about 100 μg/ml of a commercially available endotoxin, human plasma derived from rheumatism, human plasma derived from systemic lupus erythematosus and human plasma derived from myasthenia gravis), while Applicants adsorber removes

only LDL and fibrinogen from whole blood. MPEP 2143.02 makes it clear that there must be a reasonable expectation of success in the modification or combination suggested by the Office. At the time of the invention, there would not have been any reasonable expectation of success that the adsorber used to remove a wide variety of components from plasma could successfully be used to remove fibrinogen and LDL from whole blood. As an adsorber that works for whole blood may not work for plasma and the Office has not made any showing of such. As such, it would not have been obvious to one of skill in the art to use the methods and device of Hajime to treat whole blood, as set forth by claim 1.

In view of the foregoing, Tani is not obvious over present claim 1. Likewise, dependent claims 2-6 and 9-16 are also patentable over Tani for at least the same reasons as claim 1. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

Claims 7-8 and 17-18 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Tani in view of Kuroda ('449). Applicant respectfully traverses this rejection.

Claims 7-8 and 17-18 depend from claim 1, and as such includes all the limitations thereof, and is therefore patentable over Tani and Kuroda for at least the same reasons discussed above with regard to claim 1.

Accordingly, Tani in view of Kuroda is not obvious over present claims 7-8 and 17-18. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call Lawrence J. McClure or the undersigned at the Los Angeles, California telephone number (310) 785-4617 to discuss the steps necessary for placing the application in condition for allowance.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,
HOGAN & HARTSON L.L.P.

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